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09/815,923	03/23/2001	Sarjeet Gill	02307O093800	9534

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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/815,923	Applicant(s) GILL ET AL.	
File Copy	Examiner Jon D Epperson	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-5 (in part), 6-10, 11-12 (in part)* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2 (in part), 4 (in part) and 11-12 (in part)* is/are rejected.

7)☒ Claim(s) *3,5 (in part)* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on May 12, 2003 (Paper No. 10).

Priority Claims

2. No foreign or domestic priority is claimed. Therefore, the effective filing date of the claims is the filing date of the case i.e., March 23, 2001.

Status of the Claims

3. Claims 1-12 are pending in the present application.

4. Applicant's response to the Restriction and/or Election of Species requirements in Paper No. 10 is acknowledged (Applicants elected Group I, 1-5 (in part) and 11-12 (in part) with traverse wherein claims 1-5 and 11-12 read only on SEQ ID Nos. 3-4) and claims 1-5 (in part) and 11-12 (in part) and 6-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim (see below i.e., ***Response to Restriction and/or Election of Species***).

5. Therefore, claims 1-5 (in part) and 11-12 (in part) are examined on the merits in this action. Please note that claims 1-5 (in part) and 11-12 (in part) are only examined to the extent of the elected species and/or subject matter (see MPEP § 803.02).

Response to Restriction and/or Election of Species

6. Applicant's election of Group I (claims 1-5 and 11-12) in Paper No. 11 is acknowledged.

7. The traversal is on the ground(s) that "the inventions of the present application can readily be searched without undue burden because a search for one of the groups will identify art pertaining to the other" (See Paper No. 10, page 2).

8. These arguments were fully considered but were not found persuasive. As stated in the Restriction Requirement dated February 9, 2003 (Paper No. 8), these inventions (Groups I-IV) have acquired a separate status in the art as shown by their different classification and/or divergent subject matter. The different methods and/or products would require different searches in both the patent and non-patent databases (i.e., the Groups have non-overlapping subject matter that would be burdensome for the examiner to search), and there is no expectation that the searches would be coextensive. Therefore, this does create an undue search burden for the Office.

9. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

10. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

Specification

11. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Objections to the Claims

12. Claims 3 and 5 are objected to as being dependent upon a rejected base claims, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-2, 4 and 11-12 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

The claims are drawn to polypeptides (and nucleic acids encoding said polypeptides) having greater than about 70% amino acid sequence identity with the SEQ ID No. 4 polypeptide. The claims do not require that the polypeptides (with 70% homology) possess any particular conserved structure e.g., consensus sequence. Furthermore, the specification does not provide any structure/activity relationship. Thus, the claims are drawn to a genus of polypeptides that are defined solely by their sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. Here, the only identifying characteristic is a recitation of the percent homology to SEQ ID No. 4. The specification does not identify any particular portion of SEQ ID No. 4 that must be conserved for it to retain its function (i.e., as an insect cell membrane transporter) and it also does not provide a disclosure of a structure/function relationship. Consequently, the Examiner

contends that it is not possible to determine *a priori* all the different polypeptides that should be included in this genus (i.e., that have ~70% homology AND that possess the functional properties of an insect cell membrane transporter) because there is no structure/activity relationship that would allow a person of skill in the art to make this determination i.e., there is no teaching that would allow a person of skill in the art to determine *a priori* ***all*** the different types of compounds that should be included in this broad genus from the one example (i.e., SEQ ID No.4) provides by applicants.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify all the members of the genus or even a substantial portion thereof, and because the genus is highly variant listing one example (i.e., SEQ ID NO. 4) alone is insufficient to teach the entire genus. Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe this enormous genus. Thus, applicant was not in possession of the claimed genus.

Furthermore, with respect to adequate disclosure Applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires *representative examples*, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention*. See *In re Riat*_(CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re*

Barr (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University *of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure.

Here, Applicants provide only one Example (i.e., SEQ ID No. 4) that falls within the scope of Applicants' claims. This is not "representative" of the enormous number of polypeptides and/or nucleic acids encoding said polypeptides that would fall within Applicants' broad claims.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

14. Claims 1, 4 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for protein of SEQ ID NO: 4 and the nucleic acid SEQ ID NO:3 encoding said protein, does not reasonably provide enablement for protein (and nucleic acid encoding said protein) which is greater than about 70% identical to SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is an Enablement rejection.

It is clear from applicant's specification how one might practice this invention with protein with SEQ ID NO. 4 (and the nucleic acid encoding said protein i.e., SEQ ID NO. 3); however, there is insufficient guidance for proteins with greater than about 70% homology to SEQ ID NO. 4. There are many factors to be considered when determining

whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to any proteins (and nucleic acids encoding said proteins) that are "greater than about 70%" homologous to SEQ ID NO. 4. The claims are very broad in scope because every position of the protein may be mutated and more than one mutation may be included with the caveat that the protein retain ~70% homology. Furthermore, Applicants use of "comprising" terminology further broadens the scope because additional amino acids may be added to the sequence. Thus, the scope of Applicants' claims includes almost an unlimited number of "protein variants" wherein no distinguishing structural attributes are provided for the members of this genus. Given the breadth of applicants claim the nature of said invention cannot be ascertained.

(3 and 5) The state of the prior art and the level of predictability in the art:

The state of the prior art as exemplified by Attwood et al. (Attwood, T. K.; Miller, C. J. "Which craft is best in bioinformatics" *Computers and Chemistry* **2001**, *25*, 329-

339) is such that "...we do not fully understand the rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given knowledge only of its sequence or structure in isolation" (see Abstract and entire publication). Furthermore, Ponting (Ponting, C. P. "Issues in predicting protein function from sequence" Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29) states that "...predicting function by homology is a qualitative, rather than quantitative, process and requires particular care to be taken ... due attention should be paid to all available clues to function, including orthologue identification, conservation of particular residue types, and the co-occurrence of domains in proteins" (See Abstract and entire publication).

Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the proteins' function. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic and blood flow blockages (see Voet, D. and Voet, J. G. Biochemistry. New York: John Wiley and Sons 1995, pages 126-128, section 6-3A and page 230, column 2, first paragraph).

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants has provided one example of a protein that falls with the genus

claims of ~>70% homology to SEQ ID NO. 4 (i.e., Applicants have provided only SEQ ID NO. 4). No other proteins that fall within this genus have been provided.

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: The quantity of experimentation would be great because the art is inherently unpredictable (see section 3/5 above) and Applicants have provided only one example with no general teaching (i.e., structure/function relationship) that would allow extrapolation of that single example to other members of the genus. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1, 4, 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Demchyshyn et al (Demchyshyn, L. L.; Pristupa, Z. B.; Sugamori, K. S.; Barker, E. L.; Blakely, R. D.; Wolfgang, W. J.; Forte, M. A.; Niznik, H. B. "Cloning, expression, and localization of a chloride-facilitated, cocaine-sensitive serotonin transporter from Drosophila melanogaster" *Proc. Natl. Acad. Sci. USA* **May 1994**, *91*, 5158-5162).

For ***claims 1, 4, 11-12***, Demchyshyn et al discloses a 3.1-kb complementary DNA clone (dSERT) that encodes for a serotonin (5HT) transporter from *Drosophila melanogaster* wherein the encoded transporter protein is 74.3% homologous to Applicant's disclosed SEQ ID No. 4 (see Demchyshyn et al, abstract, figure 1), which anticipates claim 1.

Allowable Subject Matter

16. No claims are allowed. However, claims 3 and 5 would be allowable (to the extent that they read on SEQ ID Nos. 3 & 4) if rewritten in independent form including all of the limitations of the base claim and any intervening claims to overcome the objections to being dependent upon a rejected base claim.

Contact Information

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.
July 25, 2003

BENNETT CELSA
PRIMARY EXAMINER